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10/561,631	10/31/2006	Sonja Bromer	1131-15-PCT-PA-TD	9726
22145 7590 09/01/2010 KLEIN, O'NEILL & SINGH, LLP 18200 VON KARMAN AVENUE SUITE 725 IRVINE, CA 92612				
EXAMINER				
FRAZIER, BARBARA S				
ART UNIT		PAPER NUMBER		
1611				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/561,631

Applicant(s)

BROMER ET AL.

Examiner

BARBARA FRAZIER

Art Unit

1611

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 8-11 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-7 and 12-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/GS/US)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

DETAILED ACTION

Status of Claims

1. Claims 1-16 are pending in this application.
2. Addition of new claims 12-16 is acknowledged.
3. Applicant's affirmation of the election of Group II claims 2-7 in the reply filed on 6/16/10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
4. Claims 1 and 8-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/16/10.
5. Claims 2-7 and 12-16 are examined.

Drawings

6. The drawings were received on 6/16/10. These drawings are acceptable.

Specification

7. The objection to the specification as failing to provide proper antecedent basis for the claimed subject matter in claim 4 is withdrawn in view of Applicant's amendment to claim 4.
8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction

of the following is required: Claim 7 claims the oil emulsion according to claim 2, characterized by containing **up to 1.5%** by weight of the emulsifier, based on the total composition (see claim 7). However, the specification teaches that the content of emulsifier is **from 0.6 to 1.5%** by weight, based on the total emulsion (page 8, lines 18-20). The Examiner suggests incorporating the subject matter of claim 7 into the specification, or amending claim 7 to be consistent with the specification as currently written.

Claim Objections

9. The objection to claims 5-7 under 37 CFR 1.75(c) as being in improper form, because a multiple dependent claim cannot depend from any other multiple dependent claim, is withdrawn in view of Applicant's amendments to claims 5-7.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. **Claims 2, 5-7, and 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claim 2 as amended recites, "at least one of progestagens and estrogens" (line 3 of claim 2). It is not clear if the claim requires at least **one** of progestagens and estrogens, that is, wherein at least one progestagen or at least one estrogen must be

present, or if the claim requires at least one of progestagens **and** estrogens, that is, wherein at least one progestagen and at least one estrogen must be present.

Therefore, the metes and bounds of the claim are unclear.

Dependent claims 5-7 and 12-16 depend from claim 2 and do not clarify if one or both progestagens and estrogens must be present, and therefore are also rejected.

12. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 6 recites the broad recitation "medium chain triglycerides (MCT) having a chain length of from 6 to 12

[carbon atoms]", and the claim also recites "preferably from 8 to 10" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

13. The rejection of claims 2 and 3 under 35 U.S.C. 102(b) as being anticipated by Heckenmuller et al (WO 94/22426) is withdrawn in view of Applicant's amendment to claim 2.
14. The rejection of claim 2 under 35 U.S.C. 102(b) as being anticipated by Trotter et al (J. Clin. End. Metab. 84(12), 4531-4535, 1999) is withdrawn in view of Applicant's amendment to claim 2.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. The rejection of claim 4 under 35 U.S.C. 103(a) as being unpatentable over Heckenmuller et al (WO 94/22426) is withdrawn in view of Applicant's amendment to claim 2, from which claim 4 depends.
17. The rejection of claims 3 and 4 as being unpatentable over Trotter et al (J. Clin. End. Metab. 84(12), 4531-4535, 1999) is withdrawn in view of Applicant's amendment to claim 2, from which claims 3 and 4 depend.

18. Claims 2-7 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simon et al (EP 391396, cited by Applicants) in view of Trotter et al (J. Clin. End. Metab. 84(12), 4531-4535, 1999, cited by Applicants).

The claimed invention is drawn to a hormone-containing isotonic oil emulsion for intravenous administration comprising at least one of progestagens and estrogens; an oil phase; an antioxidant; an emulsifier; and an aqueous phase; wherein the at least one of the progestagens and estrogens are dissolved in the oil phase prior to being mixed with the aqueous phase (see claim 2).

Simon et al teach medicinal oil-in-water emulsions comprising an effective amount of a lipophilic drug, MCT oil optionally in combination with vegetable oil, about 0.05-20% of phospholipid (emulsifier), about 0.03-10% of a non-ionic surfactant (co-emulsifier) and about 0.05-5% of an ionic surfactant (co-emulsifier) (abstract). The compositions may further comprise an antioxidant such as α -tocopherol (page 5, lines 1-2); compositions comprising α -tocopherol are exemplified (Examples 1 and 2). The compositions are suitable for parenteral administration (page 4, lines 9-10), including intravenous administration (page 5, lines 19-22). Suitable hydrophobic drugs include lipophilic steroids such as progesterone (page 5, lines 3-8). The compositions may be prepared by preparing an oily solution comprising oily carrier and hydrophobic drug, and then mixing the oily solution with the aqueous solution (see page 5, lines 23-34).

While Simon et al teach that progesterone may be one of the lipophilic drugs employed in the emulsion, Simon et al do not specifically teach an emulsion containing progesterone and/or an estrogen.

Trotter et al teach an oil-in-water emulsion of an estradiol (an estrogen) and pregn-4-ene-3,20-dione (progesterone, a progestagen) in a phospholipid-stabilized soybean oil emulsion, administered as an IV infusion (see page 4532, 1st column). Trotter et al teach that administration of progesterone and estradiol in extremely preterm infants provides benefits including improved bone mineral accretion and less chronic lung disease (abstract and page 4535).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to administer progesterone and estradiol in the oil-in-water emulsion of Simon et al; thus arriving at the claimed invention. One skilled in the art would be motivated to do so because the administration of progesterone and estradiol provides the benefits of improved bone mineral accretion and less chronic lung disease, as taught by Trotter et al. One would reasonably expect success from the administration of progesterone and estradiol in the oil-in-water emulsion of Simon et al because Simon et al fairly teach and suggest that lipophilic steroids, including progesterone, may be used in its emulsion, and because Trotter et al teach that progesterone and estradiol may be administered in phospholipid-stabilized oil-in-water emulsions.

Regarding claim 3, Trotter et al teach that the concentration of estradiol is between 2.2 ng/ml and 0.22 mg/ml, and the concentration of pregn-4-ene-3,20-dione is

between 0.4 ug/ml and 1.25 mg/ml (page 4532, 1st column). These concentrations result in ratios of 6.25:1 (1.25 mg/ml to 0.22 mg/ml) and 181:1 (0.4 ug/ml to 2.2 ng/ml). These ratios are within Applicant's range of from 2:1 to 200:1.

Regarding claim 4, Trotter et al teach that the concentration of estradiol is between 2.2 ng/ml and 0.22 mg/ml (which is equivalent to 0.00000022 – 0.022% by weight), and the concentration of pregn-4-ene-3,20-dione is between 0.4 ug/ml and 1.25 mg/ml (which is equivalent to 0.00004 – 0.125% by weight (page 4532, 1st column). These amounts overlap those of the claimed invention; one skilled in the art would be motivated to manipulate the amounts of estradiol and progesterone within said ranges by routine experimentation, in order to optimize the efficacy of the resultant composition.

Regarding claim 5, Trotter et al teach that the active agents used are progesterone and estradiol (abstract and page 4532).

Regarding claim 6, Simon et al teach use of mid chain triglycerides (abstract) such as Miglyol 812 (C8-C10 triglycerides) (page 4, lines 30-31).

Regarding claim 7, Simon et al teach amounts of phospholipid of 0.05-20% (abstract). This range overlaps that of the claimed invention; one skilled in the art would be motivated to manipulate the amount of phospholipid from within said ranges by routine experimentation, in order to optimize the stability of the resultant composition.

Regarding claims 12 and 13, Simon et al teach amounts of non-ionic surfactant of 0.03-10% and ionic surfactant of 0.05-5% (abstract). These amounts overlap those of the claimed invention; one skilled in the art would be motivated to manipulate the

amount of phospholipid from within said ranges by routine experimentation, in order to optimize the stability of the resultant composition.

Regarding claim 14, Simon et al teach that the compositions may further comprise an antioxidant such as α -tocopherol (page 5, lines 1-2).

Regarding claim 15, Simon et al exemplify amounts of α -tocopherol of 0.05% of the emulsion, and 20.55% of oil phase (Example 1). Therefore, the amount of α -tocopherol would be equivalent to 0.24% of the oil phase, or 240 mg based on 100 g of the oil phase. This amount is within Applicant's range of 10mg to 1000mg based on 100g of the oil phase.

Regarding claim 16, Simon et al teach that the more preferred pH is 6.0-8.0, especially for parenteral administration (page 4, lines 28-29).

Response to Arguments

19. Applicant's arguments with respect to claims 2-4 have been considered but are moot in view of the new ground(s) of rejection. However, since the Examiner has retained the Trotter et al. reference, the Examiner will respond to arguments pertaining to said reference.

In response to Applicant's arguments that Trotter fails to disclose each and every element of the pending claim (page 10 of Remarks), it is noted that the claims are now rejected over Simon et al in view of Trotter, as delineated above.

In response to Applicant's arguments regarding claims 3 and 4 in view of Trotter (pages 11-12 of Remarks), it is noted that the previous and instant rejections point out

the teachings of Trotter regarding the amounts of estradiol and progesterone used. The instant rejection has re-calculated these amounts to demonstrate that said amounts overlap those of the claimed invention, and one skilled in the art would be motivated to manipulate the amounts within said ranges by routine experimentation, in order to optimize the efficacy of the resultant composition.

Conclusion

No claims are allowed at this time.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

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